

CLAIMS

1. An antibody recognizing both an enzyme and a substrate thereof, wherein said antibody is a
5 bispecific antibody which functionally substitutes for a cofactor that enhances the enzymatic reaction.
2. The antibody according to claim 1, wherein said enzyme is a proteolytic enzyme.
3. The antibody according to claim 2, wherein said proteolytic enzyme, substrate, and cofactor are blood coagulation/fibrinolysis-associated factors.
- 10 4. The antibody according to claim 3, wherein the enzyme of a blood coagulation/fibrinolysis-associated factor is blood coagulation factor IX and/or activated blood coagulation factor IX; the substrate is blood coagulation factor X; and the cofactor is blood coagulation factor VIII and/or activated blood coagulation factor VIII.
- 15 5. The antibody according to any one of claims 1 to 4, wherein said antibody comprises a complementarity determining region comprising the amino acid sequence of anti-blood coagulation factor IX/IXa antibody CDR3 of the following (a1) or (a2) or a complementarity determining region functionally equivalent thereto, and a complementarity determining region comprising the amino acid sequence of anti-blood coagulation factor X antibody CDR3 described in any one of the following (b1) to (b9) or a complementarity determining region
20 functionally equivalent thereto:
 - (a1) H chain CDR 3 amino acid sequence described in SEQ ID NO: 16;
 - (a2) H chain CDR 3 amino acid sequence described in SEQ ID NO: 20;
 - (b1) H chain CDR 3 amino acid sequence described in SEQ ID NO: 24;
 - (b2) H chain CDR 3 amino acid sequence described in SEQ ID NO: 28;
 - 25 (b3) H chain CDR 3 amino acid sequence described in SEQ ID NO: 32;
 - (b4) H chain CDR 3 amino acid sequence described in SEQ ID NO: 36;
 - (b5) H chain CDR 3 amino acid sequence described in SEQ ID NO: 40;
 - (b6) H chain CDR 3 amino acid sequence described in SEQ ID NO: 44;
 - (b7) H chain CDR 3 amino acid sequence described in SEQ ID NO: 48;
 - 30 (b8) H chain CDR 3 amino acid sequence described in SEQ ID NO: 52;
 - (b9) H chain CDR 3 amino acid sequence described in SEQ ID NO: 56.
6. The antibody according to any one of claims 1 to 4, wherein said antibody comprises a complementarity determining region comprising the amino acid sequence of anti-blood coagulation factor IX/IXa antibody CDR of the following (a1) or (a2) or a complementarity
35 determining region functionally equivalent thereto, and a complementarity determining region comprising the amino acid sequence of anti-blood coagulation factor X antibody CDR described

in any one of the following (b1) to (b9) or a complementarity determining region functionally equivalent thereto:

(a1) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 14, 15, and 16, respectively;

5 (a2) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 18, 19, and 20, respectively;

(b1) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 22, 23, and 24, respectively;

10 (b2) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 26, 27, and 28, respectively;

(b3) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 30, 31, and 32, respectively;

(b4) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 34, 35, and 36, respectively;

15 (b5) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 38, 39, and 40, respectively;

(b6) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 42, 43, and 44, respectively;

20 (b7) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 46, 47, and 48, respectively;

(b8) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 50, 51, and 52, respectively;

(b9) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 54, 55, and 56, respectively.

25 7. A composition comprising the antibody according to any one of claims 1 to 6 and a pharmaceutically acceptable carrier.

8. The composition according to claim 7, wherein said composition is a pharmaceutical composition used for preventing and/or treating bleeding, disorder accompanied by bleeding, or disorder caused by bleeding.

30 9. The composition according to claim 8, wherein the bleeding, disorder accompanied by bleeding, or disorder caused by bleeding is a disorder that arises and/or progresses as a result of an activity decrease or deficiency of blood coagulation factor VIII and/or activated blood coagulation factor VIII.

35 10. The composition according to claim 9, wherein the disorder that arises and/or progresses as a result of an activity decrease or deficiency of blood coagulation factor VIII and/or activated blood coagulation factor VIII is hemophilia A.

11. The composition according to claim 9, wherein the disorder that arises and/or progresses as a result of an activity decrease or deficiency of blood coagulation factor VIII and/or activated blood coagulation factor VIII is a disorder in which an inhibitor against blood coagulation factor VIII and/or activated blood coagulation factor VIII is generated.
- 5 12. The composition according to claim 9, wherein the disorder that arises and/or progresses as a result of an activity decrease or deficiency of blood coagulation factor VIII and/or activated blood coagulation factor VIII is acquired hemophilia.
13. The composition according to claim 9, wherein the disorder that arises and/or progresses as a result of an activity decrease of blood coagulation factor VIII and/or activated blood coagulation
- 10 factor VIII is von Willebrand's disease.
14. A method for preventing and/or treating bleeding, disorder accompanied by bleeding, or disorder caused by bleeding, wherein said method comprises the step of administering the antibody according to any one of claims 1 to 6, or the composition according to any one of claims 7 to 13.
- 15 15. Use of the antibody according to any one of claims 1 to 6 for preparing the composition according to any one of claims 7 to 13.
16. A kit used in the method of preventing and/or treating disorders according to claim 14, wherein said kit comprises at least the antibody according to any one of claims 1 to 6 or the composition according to claim 7.
- 20 17. A method of preventing and/or treating bleeding, disorder accompanied by bleeding, or disorder caused by bleeding, wherein said method comprises the step of administering the antibody according to any one of claims 4 to 6 or the composition according to any one of claims 7 to 13 in combination with blood coagulation factor VIII.
18. A kit used in the method of preventing and/or treating bleeding, disorder accompanied by
- 25 bleeding, or disorder caused by bleeding according to claim 17, wherein said kit comprises at least the antibody according to any one of claims 4 to 6, or the composition according to claim 7, and blood coagulation factor VIII.